REMARKS

Upon entry of the present amendment, claims 1-30, 32-34, and 36 will be pending. Claims 1-24 and 32-34 have been withdrawn. Claim 31 has been cancelled without prejudice. The specification has been amended to direct entry of the submitted sequence listing into the application and to amend a paragraph on page 39. Support for amended paragraph on page 39 can be found in the specification, e.g., at page 47, in description of Fig. 1. Claims 25, 27, 29, 30, and 36 have been amended. Support for amended claim 25 can be found in the specification as filed, e.g., at page 49, second paragraph and Table 1, and at page 44, last paragraph. Claims 27, 29, 30, and 36 have been amended to comply with dependency and grammatical formalities. Applicants submit that no new matter has been added.

Sequence Rule Compliance

Responsive to the Notice to Comply included in the Office Action, Applicants submit herewith a copy of the sequence listing, and an amendment directing its entry into the application. The sequence listing is being submitted via EFS-Web in a .txt computer-readable format.

Specification

The Examiner objected to the specification because "[o]n page 39 of the instant specification, the disclosure recites 'FIG. 6 is a schematic of the . . .' (p. 39, para 6), however, the instant application only contains total of three drawings" (at page 4). The specification has been amended accordingly to correctly refer to Fig. 1. Withdrawal of all objections to the specification is respectfully requested.

Rejections under 35 U.S.C. § 112, First Paragraph

The Examiner rejected claims 25-31 and 36 as allegedly failing to comply with the written description requirement (at page 5). According to the Examiner,

> The instant claims are drawn to a method that require "a test compound," and "GH/IGF-1 axis component." Without providing structural limitation for the claimed "test compound" and "GH/IGF-1 axis component," the claims are drawn to a genus of "test compound" that can be any compound, and a genus of GH/IGF-1 axis component that can by any component of the GH/IGF-1 axis. Neither the instant specification nor the claims have demonstrated common structure and/or function for the claimed genus of "test compounds" and the genus of "GH/IGF-1 axis component." In addition, no representative numbers of species for each claimed genus is provided to show possession of the claimed genus of compounds and genus of GH/IGF-1 axis components (at page 7).

Claim 25 has been amended to recite a method that includes, *inter alia*, providing a small molecule that is obtained by chemically modifying an agonist of a specific GH/IGF-1 axis component, namely GHRH, GHRH-R, GHS, GHS-R, GH, GH-R, IGF-1, IGF-1R, PI(3) kinase, PDK-1, Akt-1, Akt-2, or Akt-3 or a small molecule that is selected for structural similarity to an agonist of one of these components. These amendments recite specific species of the GH/IGF-1 axis components. The amendments also specify a common structure of the test compound, e.g., because exemplary types and molecular weights of small molecules are provided in the specification (see, e.g., page 44, last paragraph). Applicants submit that the amendments obviate the rejections of independent claim 25 and claims 26-30 and 36 that depend from claim 25. Claim 31 has been cancelled. Withdrawal of all written description rejections is respectfully requested.

Rejections under 35 U.S.C. § 112, Second Paragraph

The Examiner rejected claims 25-31 and 36 as allegedly being indefinite (at page 8). According to the Examiner:

> [c]laim 25 recites the phrase "structural similarity," which is a relative term and rendering the claim indefinite. The instant specification does not specifically

> define the term "structural similiarity." It is not clear on what basis and/or parameters the compounds are to share structural similiarities" (at page 9).

Applicants disagree. The specification provides various methods for obtaining structurally similar compounds. For example, "combinatorial chemical libraries can be produced that sample chemical compounds that are structurally or chemically related" (specification at page 54). As another example, the application describes use of structure-activity relationship (SAR) and structure-based design to generate antagonist compounds from agonist compounds (specification at page 55). Given the guidance of the specification, the term "structural similarity" is clear and claims 25-30 and 36 are definite. Claim 31 has been cancelled.

Further, the Examiner stated that "[c]laim 29 recites 'wherein a cohort of adult organism are treated and evaluated,' which is unclear as to how the adult organisms are treated and evaluated" (at page 9). Applicants submit that treating and evaluating animals is clearly described in the specification. For example, "Organismal Assays" are described in depth on pages 70-76. This is a clear description of treatment, which is also a term well-known in the art. Moreover, at page 71, the paragraph below Table 3 clearly describes evaluation of a test compound (e.g., in a cohort of animals, as recited in claim 29), while pages 72-76 further describe various evaluation criteria. Thus, the phrase "wherein a cohort of adult organisms are treated and evaluated" is a clear term, and claim 29 is definite.

Further, according to the Examiner,

> [c]laim 30 recites the phrase "decreased levels," which is indefinite because it's a relative term. Neither the instant specification nor the claims define the specific levels or relative levels the tested components (e.g. GH and/or IGF-1) have to decrease for "the test compound" to be "a modulator" (at page 9).

Applicants traverse. A relative term is not necessarily indefinite. Here, a skilled practitioner would understand that decreased levels of growth hormone and/or IGF-1 means levels lower than initial level (prior to providing the small molecule). The term "decreased levels" covers all levels lower than the initial level; the meaning is clear. Applicants request that the Examiner reconsider this rejection.

Withdrawal of all indefiniteness rejections is respectfully requested.

Rejections under 35 U.S.C. § 102(b)

The Examiner rejected claims 25-31 and 36 as allegedly being anticipated by Smith *et al.* (*Endocrine Reviews* 18:621-45, 1997) ("Smith") (at page 10). According to the Office at page 10:

> [t]he MK-0677 is a derivative of an antagonist or an agonist (p. 624, right col., para 2 and p. 625, left col., para 2), which reads on the chemically modifying an agonist of the GH/IGF-1 component of **clm 25**. The reference also teaches pituitary cell based assay, and GH hormone assay in rats and dogs (p.625, Left-right col., bridging para), which reads on step b) of **clm 25** . . . . (emphases in original).

Amended claim 25 recites, *inter alia*, methods of identifying a GH/IGF-1 axis antagonist, wherein the ability of a small molecule to antagonize activity of a specific GH/IGF-1 axis component identifies the molecule as an antagonist. In contrast, Smith discloses that MK-0677 was discovered in a study whose objective was amplification of the GH-secretory pathway (at page 621, second col.). MK-0677 was prepared by identifying a weak GH secretagogue and enhancing its potency as such (at pages 624-625, entire point B). Moreover, "MK-0677 was identified as having appropriate properties for a once-daily oral drug capable of sustaining amplification of pulsatile GH release" (at page 637, second col., emphasis added). Because Smith does not teach or suggest methods of, *inter alia*, identifying a GH/IGF-1 axis antagonist, wherein the ability of a small molecule to antagonize the activity of a specific GH/IGF-1 axis component identifies it as an antagonist, Smith does not anticipate claim 25 and claims 26-30 and 36 that depend from claim 25. Claim 31 has been cancelled. Withdrawal of all anticipation rejections is respectfully requested.

Conclusion

Applicants respectfully submit that all claims are in condition for allowance, which action is expeditiously requested. Applicants do not concede any positions of the Examiner that are not expressly addressed above, nor do the Applicants concede that there are not other good reasons for patentability of the presented claims or other claims. All amendments and withdrawals are made without prejudice and disclaimer and may be made for reasons not explicitly stated or for reasons in addition to ones stated.

Enclosed is a Petition for a Three-Month Extension of Time. Please apply the extension fee and any other charges or credits to deposit account 06-1050, referencing Attorney's Docket Number 13407-020001.

Respectfully submitted,

Date: July 3, 2007

Anna Solowiej

Anna Solowiej, Ph.D.
Reg. No. 57,093

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110
Telephone: (617) 542-5070
Facsimile: (617) 542-8906